

## WHAT IS CLAIMED IS;

1           1. A process for producing one or more human monoclonal  
2 antibodies which bind specifically to Shiga toxin or Shiga-like  
3 toxin, which comprises the following steps:

4                   (1) administering Shiga-like toxoid I or Shiga-  
5 like toxoid II as an antigen to a transgenic mouse having human  
6 genes and inducing an immune response in the transgenic mouse;

7                   (2) isolating splenocytes from the transgenic  
8 mouse following an immune response by the transgenic mouse and  
9 fusing the splenocytes to mouse myeloma cells to obtain mouse  
10 hybridomas producing human monoclonal antibodies; and

11                   (3) screening the human monoclonal antibodies  
12 to obtain the human monoclonal antibodies which bind specifically  
13 to Shiga toxin or Shiga-like toxin.

1           2. The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein the human  
3 monoclonal antibodies which bind specifically to Shiga toxin or  
4 Shiga-like toxin bind to Shiga-like toxin I.

1           3. The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein the human  
3 monoclonal antibodies which bind specifically to Shiga toxin or  
4 Shiga-like toxin bind to Shiga-like toxin II.

1           4.     The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein the human  
3 monoclonal antibodies which bind specifically to Shiga toxin or  
4 Shiga-like toxin bind to Shiga toxin.

1           5.     The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein according to step  
3 (1) the transgenic mouse having human genes is capable of  
4 expressing a diversity of human heavy and light chain  
5 immunoglobulins.

1           6.     The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein according to step  
3 (1) the transgenic mouse having human genes is capable of  
4 expressing unrearranged human heavy and light chain  
5 immunoglobulins.

1           7.     The process for producing one or more human  
2 monoclonal antibodies defined in claim 1 wherein according to step  
3 (1) the Shiga-like toxoid I or Shiga-like toxoid II antigen is  
4 intraperitoneally administered in an amount of 20 to 100  $\mu$ g on day  
5 1 to the transgenic mouse in complete Freund's adjuvant followed by  
6 weekly intraperitoneal immunizations with 5 to 20  $\mu$ g of antigen in  
7 incomplete Freund's adjuvant.

1           8. A human monoclonal antibody which binds specifically  
2 to Shiga toxin or Shiga-like toxin prepared by the process defined  
3 in claim 1.

1           9. The human monoclonal antibody defined in claim 8 that  
2 specifically binds to Shiga-like toxin II as the Shiga-like toxin.

1           10. The human monoclonal antibody defined in claim 9  
2 that specifically binds to the A-subunit of Shiga like toxin II.

1           11. The human monoclonal antibody defined in claim 9  
2 that specifically binds to the A-subunit of Shiga like toxin II and  
3 that neutralizes multiple variants of Shiga likme toxin II.

1           12. The human monoclonal antibody defined in claim 8  
2 that specifically binds to various clinical variants of Shiga-like  
3 toxin II as the Shiga-like toxin.

1           13. The human monoclonal antibody defined in claim 9  
2 that specifically binds to Shiga-like toxin II and which is  
3 selected from the group consisting of 5C12 and 3E9.

1           14. The human monoclonal antibody defined in claim 8  
2 that specifically binds to Shiga-like toxin I as the Shiga-like  
3 toxin.

15. The human monoclonal antibody defined in claim 8 that specifically binds to various clinical variants of Shiga-like toxin I as the Shiga-like toxin.

16. The human monoclonal antibody defined in claim 8 that will not elicit reaction in humans to foreign proteins.

17. A therapeutic method of treating an individual for hemolytic uremic syndrome or of protecting an individual against hemolytic uremic syndrome, said method comprising the steps of:

(a) producing one or more human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin, said human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin obtained by the following steps:

(1) administering Shiga-like toxoid I or Shiga-like toxoid II as an antigen to a transgenic mouse having human genes and inducing an immune response in the transgenic mouse;

(2) isolating splenocytes from the transgenic mouse following an immune response by the transgenic mouse and fusing the splenocytes to mouse myeloma cells to obtain mouse hybridomas producing human monoclonal antibodies; and

(3) screening the human monoclonal antibodies to obtain the human monoclonal antibodies which bind specifically to Shiga toxin or Shiga-like toxin; and

18 (b) administering the human monoclonal antibodies which  
19 bind specifically to Shiga toxin or Shiga-like toxin to the  
20 individual in a therapeutically effective amount.

1 18. The therapeutic method defined in claim 17 wherein  
2 the human monoclonal antibodies which bind specifically to Shiga  
3 toxin or Shiga-like toxin bind to Shiga-like toxin I.

1 19. The therapeutic method defined in claim 18 wherein  
2 the human monoclonal antibodies which bind specifically to Shiga  
3 toxin or Shiga-like toxin bind to Shiga-like toxin II.

1 20. The therapeutic method defined in claim 18 wherein  
2 the human monoclonal antibodies which bind specifically to Shiga  
3 toxin or Shiga-like toxin bind to Shiga toxin.

1 21. The therapeutic method defined in claim 17 wherein  
2 the hemolytic uremic syndrome is caused by a Shiga-like toxin  
3 producing bacteria.

1 22. The therapeutic method defined in claim 21 wherein  
2 the Shiga-like toxin producing bacteria is Enterohemorrhagic  
3 Escherichia coli.

1           23. The therapeutic method defined in claim 17 wherein  
2 the individual is protected from hemolytic uremic syndrome through  
3 passive immunization by administering to the individual a  
4 prophylactically effective amount of the human monoclonal  
5 antibodies which bind specifically to Shiga toxin or Shiga like  
6 toxin.

1           24. The therapeutic method defined in claim 19 wherein  
2 the human monoclonal antibodies which bind specifically to Shiga  
3 like toxin II specifically bind to the A-subunit of Shiga like  
4 toxin II.

1           25. The therapeutic method defined in claim 19 wherein  
2 the human monoclonal antibodies which bind specifically to Shiga  
3 like toxin II specifically bind to the A-subunit of Shiga like  
4 toxin II and neutralize multiple variants of Shiga like toxin II.